BASF
Abteilung Toxikologie
Department of Toxicology

Report; Project No. 30C0200/8625

GLP STATEMENT

Title: Prüfung der oralen Toxizität von **2,4,6-Trianilino-p-(carbo-2´-ethyl-hexyl-1´-oxi)-1,3,5-triazine** an Ratten. Verabreichung im Futter über 3 Monate.

Title (Translation): Study of the oral Toxicity of **2,4,6-Trianilino-p-(carbo-2´-ethyl-hexyl-1´-oxi)-1,3,5-triazine** in rats after 3 month administration in the diet.

This study was conducted in accordance with "OECD Principles of Good Laboratory Practice" (Paris, 1981).

1.X.87
(Head of Experimental Toxicology)

1.10.87.
(Study Director)

BASF
Abteilung Toxikologie
Department of Toxicology

Report; Project No. 30C0200/8625

STATEMENT

OF THE QUALITY ASSURANCE UNIT

Number of test substance: 86/200

Name of test substance: 2,4,6-Trianilino-p-(carbo-2'-ethyl-hexyl-1'-oxi)-1,3,5-triazine

Title: Bericht über die Prüfung der oralen Toxizität von 2,4,6-Trianilino-p-(carbo-2'ethyl-hexyl-1'-oxi)-1,3,5-triazine an Ratten. Verabreichung im Futter über 3 Monate.

Title (Translation): Report on the Study of the oral Toxicity of 2,4,6-Trianilino-p-(carbo-2'-ethyl-hexyl-1'-oxi)-1,3,5-triazine in rats after 3-month administration in the diet

The Quality Assurance Unit inspected the study, audited the final report, and reported findings to the Study Director and to Management.

Phase of study/ inspection	Date of inspection	Report to Study Director and to Management
Protocol:	Oct. 6, 1986	Oct. 20, 1986
Conduct of study:	Oct. 20, 1986	Oct. 20, 1986
	Jan. 5, 1987	Jan. 5, 1987
	Jan. 7, 1987	Jan. 7, 1987
Audit of the report:	Sep. 29, 1987	Sep. 29, 1987

Remarks: The conduct of analytics was inspected independently by the Quality Assurance Unit of the analytical laboratory.

Ludwigshafen, Oct. 1, 1987

.....
Dr.rer.nat. H. Fleig
(Head of Quality Assurance Unit

BASF
Abteilung Toxikologie
Department of Toxicology

CONTENTS

BASF
Abteilung Toxikologie
Department of Toxicology

Annex: Summary Tables

PATHOLOGY

All pathology data can be found in a separate PATHOLOGY REPORT.

The tables of the individual values and findings from the clinical and clinicochemical/hematological examinations, as well as the analytical report, can be found in Volume II.

BASF
Abteilung Toxikologie
Department of Toxicology

1. SUMMARY

2,4,6-Trianilino-p-(carbo-2´-ethyl-hexyl-1´-oxi)-1,3,5-triazine (TCT) was administered to 10 male and 10 female Wistar rats each via their diet in 3 different doses (1,000; 4,000 and 16,000 ppm) for 3 months. For comparison, one group of untreated animals (10 males and 10 females) was used as control.

Feed consumption and body weight were determined once a week; the state of health was checked each day; when the animals were weighed, they were also inspected and palpated.

At the beginning and toward the end of the study, ophthalmological examinations were carried out in the animals of the control and 16,000 ppm groups.

93 days after the beginning of administration, blood samples were taken for clinicochemical and hematological examinations.

At the end of the 3-month administration period, all animals were sacrificed by decapitation after they had been anesthetized by CO_2 and were assessed by gross pathology.

Subsequently, a histopathological examination was carried out.

No changes were detected indicating a substance-induced adverse effect. All three doses tested (16,000; 4,000 and 1,000 ppm) were thus well tolerated by the rats without any impairment of the general state or without any adverse effect on the behavior.

Body weight gain was parallel to that of the control animals. The hematological and clinicochemical examinations did not indicate any differences compared to the controls. Neither the weight parameters determined at necropsy nor the gross-pathological or histopathological examinations revealed any changes in the animals which may be due to the test substance administered.

Throughout the study period, the daily test substance intake in the highest dose group which was given 16,000 ppm of TCT in the feed was, on an average, 1,137 mg/kg body weight (between 1,664 mg/kg body weight at the beginning of the study and 882 mg/kg body weight at the end of the study) for males and 1,275 mg/kg body weight (1,682 mg/kg body weight at the beginning of the study and 1,092 mg/kg body weight at the end of the study) for females.

In summary, it may be stated that no toxicity was detected for TCT in a dose range higher than 1,000 mg/kg body weight/day, on an average.

2. *INTRODUCTION AND REASONS FOR DOSES*

The objective of the study was to determine the toxicological profile of TCT, including the target organs, after 3-month administration via the diet and to determine the no adverse effect level. The doses were chosen on the basis of the results of a test feeding study (project No. 10C0200/8629).

In this test feeding study over 14 days, the administration of the test substance in doses of 10,000 and 20,000 ppm to 3 animals per dose group and sex in their feed did not lead to any obvious effects.

Therefore, 16,000 ppm was selected as the highest dose for the 3-month administration via the diet.

This dose (16,000 ppm) was to guarantee that an amount of test substance higher than 1,000 mg/kg body weight per day was taken in and was selected as the highest dose based on the minimum dose recommended in the OECD Guidelines for a limit test for subacute and subchronic studies.

A factor of 4 was selected for fixing the further doses of 4,000 ppm and 1,000 ppm. At these dose levels, the daily test substance intake was to be $\geq$ 250 and 60 mg test substance per kg body weight respectively.

The study was carried out from Oct. 6, 1986 (beginning of administration) to Jan. 8, 1987 (beginning of necropsy) based on the OECD Guidelines for Testing of Chemicals, method No. 408.

BASF
Abteilung Toxikologie
Department of Toxicology

3. MATERIAL AND METHODS

3.1. Test substance

Name of test substance:	2,4,6-Trianilino-p-(carbo-2'-ethyl-hexyl-1'-oxi)-1,3,5-triazine
Test substance No.:	86/200
Batch number:	18301/142
Code name:	TCT
Physical state:	Solid/white powder
Stability on storage at room temperature:	Guaranteed throughout the study
Degree of purity:	$\geq$ 98%
Storage conditions:	Cool (+ 4°C)

Details on the test substance can be found with the raw data.

3.2. Test animals

Male and female Wistar rats (Chbb = Thom (SPF)), supplied by Dr. Karl THOMAE, Biberach an der Riss, FRG, which were free from any clinical signs of disease, were used for the investigations. Arrival of the animals on Sept. 30, 1986.

The rats were identified clearly by ear tattoo. The unit digit of the animal number was tattooed onto the outside of the left ear and the ten digit into the inside of the left ear.

3.3. Housing and diet

During the study period, the rats were housed singly in type DK III stainless steel wire cages supplied by BECKER & CO., Castrop-Rauxel, FRG (floor area about 900 cm^2).

The cages with the test animals were arranged on the racks in such a way that uniform experimental conditions (supply air/waste air/light) were guaranteed.

The animals were accommodated in fully air-conditioned rooms in which central air conditioning guaranteed a range of temperature of 20 - 24°C and a range of relative humidity of 30 - 70%. There were no deviations from these limits.

The day/night rhythm was 12 hours (12 hours light from 6.00 - 18.00 hours and 12 hours darkness from 18.00 - 6.00 hours).

Before the study started, the room was completely disinfected using a disinfecting apparatus ("AUTEX" fully automatic final disinfecting apparatus using formaldehyde and ammonia). Each week the walls were cleaned once and the floor was cleaned twice with water containing 0.1% Incidin perfekt (supplied by HENKEL).

The feed used was ground Kliba maintenance diet rat/mouse/hamster, GLP 343 meal, supplied by Klingentalmühle AG, CH-4303 Kaiseraugst, Switzerland, which was available to the animals ad libitum throughout the study period, as was drinking water.

3.4. Test groups and doses

Test group	Concentration ppm	Number of animals male	female
0	0	10	10
1	1,000	10	10
2	4,000	10	10
3	16,000	10	10

3.5. Analysis

The investigations were carried out in the analytical laboratory of BASF Aktiengesellschaft (Dr. Mandery responsible).

3.5.1. Analysis of test substance

The test substance was characterized before the start of the study. To check the stability of the test substance over the entire study period, it was reanalyzed at the end of the study.

3.5.2. Analysis and preparation of test substance preparations

Test substance preparations were prepared at least once a month. Before the beginning of the study, the stability of the test substance in the diet for a period of 32 days at room temperature had been demonstrated.

The amount of test substance weighed was thoroughly mixed with a small portion of the feed, using a spatula and subsequently mixed using a BOSCH mixer. This premix was then adjusted to the concentration desired with the appropriate amount of feed and mixed in a laboratory mixer of GEBR. LÖDIGE for about 10 minutes.

To verify the homogeneous distribution of the test substance in the feed, samples were sent for analysis at the start and in the 8th week of the study.

To verify the correctness of weighings, samples were sent for analysis at the start, in the 8th week and at the end of the study.

The samples scheduled for analysis were stored in the laboratory at - 18^{0}C until they were analyzed.

3.5.3. Methods

The content of TCT in the test substance/feed mixtures was determined by HPLC.

More details about the method used are to be found with the raw data.

3.5.4. Analysis of feed

The feed used in the study was assayed for contaminants.

3.5.5. Analysis of drinking water

The drinking water was regularly assayed for contaminants both by the municipal authorities of Frankenthal and by the Department of Water Chemistry and Technical Services of BASF Aktiengesellschaft.

3.6. Experimental procedure

The animals were 36 days old when supplied, and a 6-day acclimatization period started during which they were accustomed to their surroundings.

3 days prior to the start of the study, the male and female mice were allocated to the individual test groups according to weight and separately according to sex. The list of randomization instructions was compiled with a computer (laboratory data processing, Department of Toxicology, BASF Aktiengesellschaft).

At the beginning of the administration period, the animals were 42 days old and the mean body weight was as follows:

- male animals: 203 (188 - 213) g
- female animals: 158 (145 - 172) g.

At the end of the 3-month administration period, all animals were sacrificed following a fasting period.

3.7. Clinical examinations

3.7.1. Feed consumption, body weight and body weight change

The feed consumption and body weight of the animals were determined once a week (Mondays) from the beginning of the administration period onward. Furthermore, for randomization of the animals, the body weight was determined 3 days before the beginning of the administration period.

The body weight change was calculated for each individual animal according to the following formula using the computer systems of the Department of Toxicology of BASF Aktiengesellschaft (laboratory data processing, Dr. H. D. Hoffmann responsible).

$$BW_{day\ x} - BW_{day\ 0}$$

$BW_{day\ x}$ = body weight on day x of study (in g)

The values listed in the tables are group means determined from the body weight gains/losses of the individual animals.

3.7.2. Feed efficiency

The feed efficiency was calculated for each individual animal at the intervals at which body weight and feed consumption were simultaneously determined, using the following formula:

$$\frac{BW_{day\ x} - BW_{day\ x-7}}{FC_{day\ x-7\ to\ day\ x}} \times 100$$

$BW_{day\ x}$ = body weight on day x of study (in g)

$BW_{day\ x-7}$ = body weight on day x-7 (in g)

$FC_{day\ x-7\ to\ day\ x}$ = feed consumption withon one week of the study from day x-7 to day x (in g)

The values listed in the tables are group means determined from the feed efficiencies of the individual animals.

3.7.3. Test substance intake

The mean daily intake of test substance (in mg) per kg of body weight was calculated for each individual animal at the intervals at which feed consumption was determined.

The calculation was carried out according to the following formula using the computer systems of the Department of Toxicology of BASF Aktiengesellschaft (laboratory data processing, Dr. H. D. Hoffmann responsible).

$$\frac{FC \times D}{BW_x}$$

FC = mean daily feed consumption (in g) within one week of the study (from day x-7 to day x)

D = dose in ppm

BW_x = body weight on day x of study (in g)

The values listed in the tables are group means determined from the intakes of test substance by the individual animals.

3.7.4. Clinical signs

The animals were examined daily for any externally evident signs of toxicity. Furthermore, additional inspection and palpation of the animals were carried out once a week (Mondays).

3.7.5. Mortality

A check was made twice (Mondays to Fridays) or once a day (Saturdays, Sundays and public holidays) for any dead or moribund animals.

3.7.6. Ophthalmological examinations

At the beginning of the administration period and at the end of the study, the eyes of the animals in test group 0 (control) and in test group 3 (16,000 ppm) were examined with a focusable hand slit lamp (1) for any changes to the refracting media.

In the ophthalmological examination at the end of the study, some animals of test groups 0 and 3 were additionally subjected to a fundus examination using a Kowa camera (2).

(1) HEINE-Focalux hand slit lamp

3.8. Clinical chemistry and hematology

3.8.1. Blood and plasma examinations

The blood required was taken from the retroorbital venous plexus of the non-fasted animals in the morning.

The blood samplings and the subsequent analysis of the blood and plasma samples were carried out, with the exception of the differential blood counts, in a randomized sequence 93 days after the beginning of administration (blood sampling 1). The list of randomization instructions was compiled with a computer using a random-number generator. The clinicochemical and hematological examinations were carried out in 10 animals per test group and sex.

The following clinicochemical and hematological parameters were determined:

3.8.1.1. Hematological examinations

The following parameters were determined using a particle counter (Coulter Counter, S Plus model):

- leukocytes
- erythrocytes
- hemoglobin
- hematocrit
- mean corpuscular volume
- mean hemoglobin content per erythrocyte
- mean corpuscular hemoglobin concentration
- platelets

The data were transferred to a computer (VAX 11/780; supplied by DEC, Munich, FRG).

The differential blood count was evaluated using an automatic differential system (HEMATRAK 480 model, supplied by Geometric Data, Munich, FRG). The data were entered off-line into the computer.

The methods used can be seen from the following table:

BASF
Abteilung Toxikologie
Department of Toxicology

HEMATOLOGY

Parameter	Unit	Method	References
Leukocytes (WBC)	giga/l	measured according to Coulter principle	Coulter Counter instructions; laboratory modification
Erythrocytes (RBC)	tera/l	measured according to Coulter principle	
Hemoglobin (HGB)	mmol/l	hemiglobin cyanide; photometric measurement; 525 nm	
Hematocrit (HCT)	l/l	calculation: $\frac{MCV \cdot erythrocytes}{1000}$	
Mean corpuscular volume (MCV)	fl	measured according to Coulter principle	
Mean hemoglobin content per erythrocyte (MCH)	fmol	calculation: $\frac{hemoglobin}{erythrocytes}$	
Mean corpuscular hemoglobin concentration (MCHC)	mmol/l	calculation: $\frac{hemoglobin}{hematocrit}$	
Platelets (PLT)	giga/l	measured according to Coulter principle	
Differential blood count	% and giga/l	staining according to Wright; microscopic evaluation	Evaluation according to: Schermer, S., "The Blood Morphology of Laboratory Animals", F.A. Davis Co, Philadelphia (1967)

3.8.1.2. Clotting analyses

The clotting analyses were carried out using a ball coagulometer (KC 10 model; supplied by Amelung, Lemgo, FRG), and the results were entered off-line into the computer.

The following parameter was determined:

- thromboplastin time (Hepato Quick's test)

The method used can be seen from the following table:

Parameter	Unit	Method	References
Thromboplastin time (Hepato Quick's test) (HQT)	seconds	citrated blood with tissue thromboplastin	Fischer, M. and Falkensammer, Ch., Klin. Wschr. 86, 577 - 583 (1974)

3.8.1.3. Clinicochemical examinations

The clinicochemical blood parameters were examined using an automatic analyzer (Hitachi 737 model; supplied by Boehringer, Mannheim, FRG). The results were transferred to a computer (VAX 11/780; supplied by DEC, Munich, FRG).

The following parameters were determined:

1. Enzymes

- alanine aminotransferase
- aspartate aminotransferase
- alkaline phosphatase

2. Blood chemistry

- sodium
- potassium
- chloride
- inorganic phosphate
- calcium
- urea
- creatinine
- glucose
- total bilirubin
- total protein
- albumin
- globulins
- triglycerides
- cholesterol

The methods used can be seen from the following table:

BASF
Abteilung Toxikologie
Department of Toxicology

1. ENZYMES

Enzyme (systematic name and system number)	Unit	Method, wavelength and measuring temperature	References
Alanine aminotransferase (ALT) (L-alanine:2-oxoglutarate aminotransferase; EC 2.6.1.2.)	µkat/l	kinetic UV test, 340 nm, 37°C	Recommendations of German Society for Clinical Chemistry: "Standardization of methods for determining enzyme activities in biological liquids" J. Clin. Chem. Clin. Biochem. 8, 658 - 660 (1970); J. Clin. Chem. Clin. Biochem. 9, 464 - 465 (1971); J. Clin. Chem. Clin. Biochem. 10, 182 - 192 (1972); BM working instructions
Aspartate aminotransferase (AST) (L-aspartate:2-oxoglutarate aminotransferase; EC 2.6.1.1.)	µkat/l	kinetic UV test, 340 nm, 37°C	
Alkaline phosphatase (ALP) (orthophosphoric acid monoester phosphohydrolase; EC 3.1.3.1.)	µkat/l	kinetic color test, 415 nm 37°C	

BM = Boehringer Mannheim, FRG

2. BLOOD CHEMISTRY

Parameter	Unit	Method	References
Sodium (NA)	mmol/l	ion selective electrodes (ISE)	Hitachi 737 - working instructions
Potassium (K)	mmol/l		
Chloride (CL)	mmol/l		
Inorganic phosphate (INP)	mmol/l	molybdate reaction	Henry, R.J. in "Clinical Chemistry", Harper and Row Publishers, New York (1974); BM working instructions
Calcium (CA)	mmol/l	o-cresolphthalein-complex without deproteinization	Ray Sarkar, B.C. and Chauhan, U.P.S., Anal. Biochem. 20, 155 (1967); BM working instructions
Urea (UREA)	mmol/l	enzymatic determination; urease/glutamic dehydrogenase method	Neumann, U. and Ziegenhorn, J.: XVI, Nordiska kongressen for klinisk kemi och klinisk fysiologi 1977, Oulu, Finland; BM working instructions
Creatinine (CREA)	µmol/l	kinetic Jaffé reaction without deproteinization	Bartels, H. et al., Clin. Chim. Acta 37, 193 (1972); BM working instructions
Glucose (GLUC)	mmol/l	hexokinase/glucose-6-phosphate-dehydrogenase method	Schmidt, F.H., Klin. Wschr. 34, 1244 - 1247 (1961); BM working instructions
Total bilirubin (TBIL)	µmol/l	DPD reaction	Wahlefeld, A.W. et al., Scand. J. Clin. Lab. Invest. 29, Suppl. 126 (1972) Abstract 11.12; BM working instructions
Total protein (TPROT)	g/l	biuret reaction	Weichselbaum, T.E., Amer. J. Clin. Path. 16, 40 (1946); BM working instructions
Albumin (ALB)	g/l	bromocresol green reaction	Doumas et al., Clin. Chim. Acta 31, 87 (1971); BM working instructions
Globulins (GLOB)	g/l	difference between total protein and albumin	
Triglycerides (TRIG)	mmol/l	enzymatic color test; lipase-esterase/ glycerokinase/glycerol-3-phosphate oxidase/ 4-aminophenazone	mod. method according to Wahlefeld, A.W. in "Methoden der enzymatischen Analyse" (Bergmeyer, H.U., ed.) Vol. II, 3rd ed. Verlag Chemie Weinheim, pp. 1878 - 1882 (1974); BM working instructions
Cholesterol (CHOL)	mmol/l	enzymatic determination; cholesterol esterase cholesterol oxidase/4-aminophenazone (CHOD-PAP method)	Siedel, J. et al., J. Clin. Chem. Clin. Biochem. 19, 838 (1981); BM working instructions

BM = Boehringer Mannheim, FRG

3.9. Statistical evaluation

The data were evaluated statistically on the computer systems of the Department of Toxicology of BASF Aktiengesellschaft (laboratory data processing, Dr. H. D. Hoffmann responsible).

3.9.1. Clinical examinations, clinical chemistry and hematology

In the statistical evaluation of the clinical, clinicochemical and hematological parameters, means and standard deviation of the individual values of the specific test groups were calculated and printed in the form of tables. In order to test if the results of the individual dose groups differ statistically significantly from the results of the control group, the means, with the exception of the differential blood counts and test substance intake, of the corresponding dose group and control group were compared using an analysis of variance (ANOVA) and Dunnett's test (1, 2).

Significances resulting from the statistical comparison have been indicated in the tables on means.

---

(1) DUNNETT, C.W. (1955):
A multiple comparison procedure for comparing several treatments with a control.
J. Amer. Statist. Assoc. 50, 1096 - 1121

(2) DUNNETT, C.W. (1964):
New Tables for multiple comparisons with a control.
Biometrics 20, 482 - 491

3.10. Pathology

For methods, see separate PATHOLOGY REPORT.

3.11. Retention of records

The study protocol, the raw data, the reserve sample and the specimens, as well as the original of the report, are stored at BASF Aktiengesellschaft for at least the period of time specified in the GLP regulations. The specimens will be retained only for as long as the quality of the material allows evaluation.

4. *RESULTS AND ASSESSMENT OF FINDINGS*

4.1. Analysis

All analyses were carried out in the Central Investigation Laboratory of BASF Aktiengesellschaft (ZHU).

4.1.1. Analysis of test substance

The stability of the test substance throughout the study period was confirmed by the reanalysis carried out at the end of the study.

A degree of purity of 98% and 99% was determined at the beginning and at the end of the study respectively.

Details may be found in the raw data.

4.1.2. Analysis of test substance preparations

The homogeneity of the test substance in the carrier could not be confirmed definitely in the analysis of the samples taken at the beginning of the study. Therefore, samples of each concentration were taken anew in the 8th week of the study and sent to the analytical laboratory.

The result of these analyses then confirmed the homogeneity of the test substance in the carrier. The same applies to the concentration control analysis carried out at the beginning of the study.

The analysis of the carrier (Kliba meal) of the samples sent for analysis in the 8th test week revealed a content of TCT of about 44 ppm, on an average. When the analysis was repeated with a carrier sample supplied additionally, no traces of the test substance were detected so that it is very likely that contamination occurred during sampling.

The correctness of the amounts weighed in was confirmed by the concentration control analysis carried out at the end of the study.

The sufficient stability of TCT in the feed for 32 days was verified at the beginning of the study.

Details may be found in the raw data.

Fig. 4.1.2.1.: Detection of test substance in the feed

Sample sent	Test group	Target value ppm	Actual value ppm
At the beginning of the study	1	1,000	737 1,275 1,091 953 825 937
	2	4,000	3,872 3,886 3,902 3,885 3,878 3,933
	3	16,000	14,679 12,204 16,605 20,752 14,748 15,443
In the 8th test week	1	1,000	972 964 952 956 961 957 968 961 982 979 1,005 1,011
	2	4,000	3,967 4,039 3,925 3,924 3,853 3,832 3,961 3,936 3,946 3,926 3,942 3,971
	3	16,000	15,186 15,166 15,397 15,393 15,563 15,602 15,055 15,137 15,378 15,375 14,978 14,934
At the end of the study	1	1,000	1,048 1,058 1,057 1,054
	2	4,000	4,128 4,145 4,155 4,142
	3	16,000	16,013 15,946 15,920 15,867

4.1.3. Analysis of feed

The feed was regarded as suitable for the intended period of use and on the basis of the results of the tests for contaminants. The Proposed Guidelines of the EPA of May 9, 1979, Fed. Reg. 44, No. 91, p. 27354, were used as a reference for maximum tolerable contaminants.

4.1.4. Analysis of drinking water

The drinking water used was regarded as suitable on the basis of the results obtained. The German Drinking Water Regulations of Jan. 31, 1975 and of May 22, 1986 were used as a reference.

4.2. Clinical examinations

The results of the study are shown in the following Summary Tables in the Annex:

	Table
Key to the abbreviations, page 30	
Feed consumption in g/animal/day	
- male and female animals	001 - 004
Body weight in g	
- male and female animals	005 - 008
Body weight change	
- male and female animals	009 - 012
Feed efficiency	
- male and female animals	013 - 016
Test substance intake in mg/kg body weight/day	
- male and female animals	017 - 020

The individual values are to be found in Part A of the tables (Volume II).

4.2.1. Feed consumption

There were no differences between the treated groups and the control group with regard to feed consumption throughout the study period (Tabs. 001 to 004).

4.2.2. Body weight/body weight change

The body weight gain of the dose groups (1,000; 4,000 and 16,000 ppm) was substantially similar to that of the specific control group (Tabs. 005 to 012).

4.2.3. Feed efficiency

Neither the males nor the females of all test groups (1,000; 4,000 and 16,000 ppm) showed any obvious differences with regard to feed efficiency compared with the specific control group (Tabs. 013 to 016).

4.2.4. Test substance intake

The amount of test substance (in mg) consumed each day by the animals per kilogram body weight was calculated at the times at which the feed consumption was determined. The group means calculated from the amounts of test substance ingested by the individual animals can be seen from Tables 017 to 020.

4.2.5. Clinical signs

The 3 doses administered as addition to the diet (1,000; 4,000 and 16,000 ppm) did not lead to any disturbances in the general behavior in any of the animals of the study.

4.2.6. Mortality

No animal died prematurely during the study period.

4.2.7. Ophthalmological examinations

The ophthalmological examinations carried out with a hand slit lamp at the beginning and end of the administration period did not show any impairment of the refracting media (see Fig. 4.2.7.1. and Fig. 4.2.7.2.). The investigation carried out in some animals with the Kowa camera did not reveal any spontaneous or substance-induced changes of the ocular fundus either. The individual findings can be seen from the raw data.

4.2.8. Conclusions

In conclusion, it may be stated that the administration of TCT did not lead to any impairment of the general behavior or of clinically relevant parameters.

Therefore, from the point of view of clinical examinations, a no observed effect level is in a range higher than 16,000 ppm.

BASF
Abteilung Toxikologie
Department of Toxicology

Fig. 4.2.7.1.

OPHTHALMOLOGICAL FINDINGS

Males

	At the beginning of the study		At the end of the study	
Test group	0 (0 ppm)	3 (16,000 ppm)	0 (0 ppm)	3 (16,000 ppm)
Number of eyes examined	20	20	20	20
Corneal stippling	0	2	1	2
Pupillary membrane residues	8	13	6	10
Water cleft formation	0	0	0	0
Lens star	2	0	0	0

In some animals several findings were recorded in one eye.

Fig. 4.2.7.2.

OPHTHALMOLOGICAL FINDINGS

Females

	At the beginning of the study		At the end of the study	
Test group	0 (0 ppm)	3 (16,000 ppm)	0 (0 ppm)	3 (16,000 ppm)
Number of eyes examined	20	20	20	20
Corneal stippling	0	0	0	1
Pupillary membrane residues	10	5	9	6
Water cleft formation	0	0	0	0
Lens star	0	0	0	0

In some animals several findings were recorded in one eye.

4.3. Clinical chemistry and hematology

The results of the study are shown, together with a key to the abbrevations, in the following Summary Tables in the Annex:

	Table
Key to the abbreviations, pages 31 + 32	
Hematological examinations	
- male animals	021
- female animals	022
Differential blood count	
- male animals	023 + 024
- female animals	025 + 026
Clotting analyses	
- male animals	027
- female animals	028
Enzymes	
- male animals	029
- female animals	030
Blood chemistry	
- male animals	031 + 032
- female animals	033 + 034

The relevant tables on the individual values are to be found in Part B of the tables (Volume II).

4.3.1 Assessment of findings

From the point of view of clinical chemistry and hematology, the 3-month administration of the test substance to rats in doses of 1,000; 4,000 and 16,000 ppm did not lead to any substance-induced changes.

The clinicochemical parameters listed below sporadically showed significant deviations from the control group. They are of no substance-induced relevance on account of the plausibility criteria described in detail below:

Parameter		Table	Plausibility criteria
UREA	(UREA)	031	B, G, H
TRIGLYCERIDES	(TRIG)	032	G, H
CALCIUM	(CA)	033	G, H
TOTAL PROTEIN	(TPROT)	034	B, F, G, H
GLOBULINS	(GLOB	034	F, G, H

Plausibility criteria

The significant deviations from the control values are not to be considered to be substance-related. Plausibility criteria have been introduced in order to avoid a detailed assessment and discussion of each individual statistically significant deviation for each parameter. The purpose of these criteria is to give all the reasons why the administration of the test substance is not relevant or is unlikely to be relevant. These plausibility criteria are listed in detail below and are assigned to the relevant parameters by the appropriate identification letters.

A) The changes have no pathognomonic relevance

B) The values lie within the range of biological variation; effect not relevant

C) Contrary change in both sexes; effect not very plausible

D) Similar effect absent for parameters which have a similar dependence on one another; not very plausible

E) Reciprocal effect absent for parameters which have a reciprocal dependence; effect not very plausible

F) Random increase or decrease in the control value; effect not relevant

G) No monotonic trend present (absence of dose-response relationship); effect not very plausible

H) Similar effect absent in both sexes; not very plausible

I) Trend within the test group; effect not relevant

K) First change in the recovery period; effect not very plausible

4.3.2. Conclusions

There were no substance-induced changes in the clinico-chemical or hematological examinations.

4.4. Pathology

For results and assessment of findings, conclusions and Summary Tables and individual data sheets, see separate PATHOLOGY REPORT.

BASF TOXICOLOGY
PROJECT NUMBER 30C0200/8625

3-MONTH FEEDING STUDY OF TCT IN RATS

GROUP MEANS

BODYWEIGHT CHANGE

PRINT DATE 28-JUL-87

M A L E S		day 7	day 14	day 21	day 28	day 35	day 42	day 49	day 56
		BW CHGE G	BW CHGE G	BW CHGE G	BW CHGE G	BW CHGE G	BW CHGE G	BW CHGE G	BW CHGE G
GROUP 0									
0 PPM	M	51.7	94.0	126.7	152.2	176.5	202.3	220.5	238.9
	SD	5.0	9.4	12.2	13.2	17.0	19.6	18.0	18.8
	N	10	10	10	10	10	10	10	10
GROUP 1									
1000 PPM	M	57.3	101.0	132.0	157.3	183.1	205.5	227.1	244.8
	SD	8.8	10.6	11.1	11.6	12.8	14.2	16.8	15.4
	N	10	10	10	10	10	10	10	10
GROUP 2									
4000 PPM	M	51.3	94.9	129.5	155.2	181.2	208.1	226.8	246.1
	SD	5.8	10.3	16.5	19.5	22.7	27.8	29.3	30.4
	N	10	10	9	10	10	10	10	10
GROUP 3									
16000 PPM	M	49.1	92.6	122.3	148.3	172.4	194.5	216.2	233.6
	SD	4.7	9.3	14.0	16.6	18.3	19.7	21.9	24.7
	N	10	10	10	10	10	10	10	10

Statistics: Anova + Dunnetts tests * P<0.05 ** P<0.01 two sided (Statistical unit = animal)

BASF TOXICOLOGY
PROJECT NUMBER 30C0200/8625 3-MONTH FEEDING STUDY OF TCT IN RATS

GROUP MEANS BODYWEIGHT CHANGE PRINT DATE 30-JUL-87

M A L E S		day 63	day 70	day 77	day 84	day 91
		BW CHGE G	BW CHGE G	BW CHGE G	BW CHGE G	BW CHGE G
GROUP 0						
0 PPM	M	257.2	270.2	284.0	294.1	307.1
	SD	22.9	24.1	24.5	34.2	29.7
	N	10	10	10	10	10
GROUP 1						
1000 PPM	M	260.3	273.7	289.4	301.6	313.0
	SD	18.5	18.9	21.7	20.2	19.9
	N	10	10	10	10	10
GROUP 2						
4000 PPM	M	259.2	274.0	287.9	301.4	313.7
	SD	34.4	36.7	39.1	39.4	45.4
	N	10	10	10	10	10
GROUP 3						
16000 PPM	M	246.0	259.2	272.7	280.9	292.9
	SD	25.2	25.3	28.6	30.8	30.1
	N	10	10	10	10	10

Statistics: Anova + Dunnetts tests * P<0.05 ** P<0.01 two sided (Statistical unit = animal)

TABLE 011

BASF TOXICOLOGY
PROJECT NUMBER 30C0200/8625 3-MONTH FEEDING STUDY OF TCT IN RATS

GROUP MEANS BODYWEIGHT CHANGE PRINT DATE 28-JUL-87

F E M A L E S		day 7	day 14	day 21	day 28	day 35	day 42	day 49	day 56
		BW CHGE G	BW CHGE G	BW CHGE G	BW CHGE G	BW CHGE G	BW CHGE G	BW CHGE G	BW CHGE G
GROUP 0									
0 PPM	M	22.4	35.9	47.3	62.2	73.7	79.6	83.4	95.4
	SD	6.3	13.0	14.2	15.9	17.7	22.0	22.3	22.1
	N	10	10	10	10	10	10	10	10
GROUP 1									
1000 PPM	M	22.7	38.0	55.2	63.5	73.2	82.3	88.5	96.9
	SD	5.2	7.1	8.4	10.8	11.4	15.1	10.4	15.4
	N	10	10	10	10	10	10	10	10
GROUP 2									
4000 PPM	M	20.8	37.5	53.1	63.1	72.2	81.8	92.3	100.6
	SD	6.8	11.7	16.5	17.0	17.3	20.4	24.2	21.2
	N	10	10	10	10	10	10	10	10
GROUP 3									
16000 PPM	M	25.7	42.4	54.0	68.2	82.2	89.4	94.4	106.3
	SD	8.6	9.5	11.7	11.7	13.2	14.4	16.9	15.0
	N	10	10	10	10	10	10	10	10

Statistics: Anova + Dunnetts tests * P<0.05 ** P<0.01 two sided (Statistical unit = animal)

BASF TOXICOLOGY
PROJECT NUMBER 30C0200/8625

3-MONTH FEEDING STUDY OF TCT IN RATS

GROUP MEANS

BODYWEIGHT CHANGE

PRINT DATE 30-JUL-87

F E M A L E S		day 63	day 70	day 77	day 84	day 91
		BW CHGE G	BW CHGE G	BW CHGE G	BW CHGE G	BW CHGE G
GROUP 0						
0 PPM	M	102.9	107.5	113.8	120.2	125.9
	SD	23.7	24.0	22.8	20.8	23.2
	N	10	10	10	10	10
GROUP 1						
1000 PPM	M	105.8	110.6	117.3	123.2	128.9
	SD	13.2	15.9	15.4	14.1	14.1
	N	10	10	10	10	10
GROUP 2						
4000 PPM	M	105.1	113.9	121.0	126.2	131.0
	SD	21.8	23.7	25.7	24.6	25.3
	N	10	10	10	10	10
GROUP 3						
16000 PPM	M	115.7	118.4	119.1	130.1	135.1
	SD	14.7	16.0	18.2	14.1	14.9
	N	10	10	10	10	10

Statistics: Anova + Dunnetts tests * P<0.05 ** P<0.01 two sided (Statistical unit = animal)

TABLE 013

BASF TOXICOLOGY
PROJECT NUMBER 30C0200/8625 3-MONTH FEEDING STUDY OF TCT IN RATS

GROUP MEANS FOOD-EFFICIENCY PRINT DATE 27-AUG-87

M A L E S		day 7	day 14	day 21	day 28	day 35	day 42	day 49	day 56
		FOOD EFF	FOOD EFF	FOOD EFF	FOOD EFF	FOOD EFF	FOOD EFF	FOOD EFF	FOOD EFF
GROUP 0									
0 PPM	M	28.4	22.2	17.3	13.8	12.8	13.8	9.9	9.7
	SD	2.4	2.1	1.2	3.4	3.0	2.9	2.8	1.6
	N	10	10	10	10	10	10	10	10
GROUP 1									
1000 PPM	M	30.1	22.1	16.1	13.4	13.4	11.8	11.1	9.2
	SD	3.1	1.2	1.4	2.1	1.3	1.5	1.7	1.6
	N	10	10	10	10	10	10	10	10
GROUP 2									
4000 PPM	M	27.5	22.1	17.5	13.9	13.3	13.6	9.5	10.0
	SD	2.9	2.4	2.8	1.8	1.7	2.3	2.0	2.4
	N	10	10	9	9	10	10	10	10
GROUP 3									
16000 PPM	M	26.8	22.4	15.3	13.7	12.4	11.4	11.0	8.9
	SD	2.0	1.8	2.2	1.5	1.5	1.9	1.4	1.5
	N	10	10	10	10	10	10	10	10

Statistics: Anova + Dunnetts tests * P<0.05 ** P<0.01 two sided (Statistical unit = animal)

BASF TOXICOLOGY
PROJECT NUMBER 30C0200/8625 3-MONTH FEEDING STUDY OF TCT IN RATS

GROUP MEANS FOOD-EFFICIENCY PRINT DATE 27-AUG-87

M A L E S		day 63	day 70	day 77	day 84	day 91
		FOOD EFF	FOOD EFF	FOOD EFF	FOOD EFF	FOOD EFF
GROUP 0						
0 PPM	M	9.6	6.9	7.0	4.7	6.7
	SD	2.2	2.9	4.2	8.4	4.3
	N	10	10	10	10	10
GROUP 1						
1000 PPM	M	8.0	7.0	7.8	6.4	5.9
	SD	2.2	1.5	2.1	3.3	1.7
	N	10	10	10	10	10
GROUP 2						
4000 PPM	M	6.6	7.4	6.8	6.8	6.2
	SD	5.8	4.0	6.4	5.4	2.9
	N	10	10	10	10	10
GROUP 3						
16000 PPM	M	6.4	6.9	6.9	4.3	6.2
	SD	0.8	2.4	2.2	2.3	2.9
	N	10	10	10	10	10

Statistics: Anova + Dunnetts tests * P<0.05 ** P<0.01 two sided (Statistical unit = animal)

TABLE 015

BASF TOXICOLOGY
PROJECT NUMBER 30C0200/8625

3-MONTH FEEDING STUDY OF TCT IN RATS

GROUP MEANS

FOOD-EFFICIENCY

PRINT DATE 27-AUG-87

F E M A L E S		day 7	day 14	day 21	day 28	day 35	day 42	day 49	day 56
		FOOD EFF	FOOD EFF	FOOD EFF	FOOD EFF	FOOD EFF	FOOD EFF	FOOD EFF	FOOD EFF
GROUP 0									
0 PPM	M	17.3	10.5	8.7	11.6	8.9	4.4	2.9	9.0
	SD	3.5	5.4	4.8	3.5	2.6	6.0	4.4	3.6
	N	10	10	10	10	10	10	10	10
GROUP 1									
1000 PPM	M	17.1	11.7	12.8	6.5*	7.1	6.8	4.3	6.0
	SD	3.7	3.7	4.5	3.9	5.6	3.8	8.3	7.4
	N	10	10	10	10	10	10	10	10
GROUP 2									
4000 PPM	M	15.1	12.4	11.2	7.5	6.8	6.9	7.1	6.2
	SD	3.4	5.2	5.2	3.6	4.3	5.6	5.2	4.6
	N	10	10	10	10	10	10	10	10
GROUP 3									
16000 PPM	M	18.7	12.4	8.4	10.3	9.9	5.4	3.5	8.5
	SD	4.4	2.4	3.3	4.7	3.2	1.8	4.5	4.3
	N	10	10	10	10	10	10	10	10

Statistics: Anova + Dunnetts tests * P<0.05 ** P<0.01 two sided (Statistical unit = animal)

BASF TOXICOLOGY
PROJECT NUMBER 30C0200/8625 3-MONTH FEEDING STUDY OF TCT IN RATS

GROUP MEANS FOOD-EFFICIENCY PRINT DATE 27-AUG-87

F E M A L E S		day 63	day 70	day 77	day 84	day 91
		FOOD EFF	FOOD EFF	FOOD EFF	FOOD EFF	FOOD EFF
GROUP 0						
0 PPM	M	5.7	3.7	4.5	4.9	4.0
	SD	3.5	2.6	4.6	5.0	4.8
	N	10	10	10	10	10
GROUP 1						
1000 PPM	M	6.3	3.4	4.8	4.2	3.9
	SD	6.5	3.5	5.2	3.8	5.4
	N	10	10	10	10	10
GROUP 2						
4000 PPM	M	3.3	6.2	5.0	3.8	3.4
	SD	2.3	3.9	2.9	4.4	2.8
	N	10	10	10	10	10
GROUP 3						
16000 PPM	M	6.8	2.0	0.4	7.7	3.5
	SD	2.6	2.1	3.6	4.4	2.6
	N	10	10	10	10	10

Statistics: Anova + Dunnetts tests * P<0.05 ** P<0.01 two sided (Statistical unit = animal)

TABLE 017

BASF TOXICOLOGY
PROJECT NUMBER 30C0200/8625

3-MONTH FEEDING STUDY OF TCT IN RATS

GROUP MEANS

SUBSTANCE INTAKE

PRINT DATE 23-JUL-87

M A L E S		day 7	day 14	day 21	day 28	day 35	day 42	day 49	day 56
		SUB.INT. MG/KG BW	SUB.INT. MG/KG BW	SUB.INT. MG/KG BW	SUB.INT. MG/KG BW	SUB.INT. MG/KG BW	SUB.INT. MG/KG BW	SUB.INT. MG/KG BW	SUB.INT. MG/KG BW
GROUP 1									
1000 PPM	M	103.9	92.7	82.4	74.7	70.8	66.1	64.3	61.6
	SD	3.9	3.1	3.7	2.9	3.0	2.6	2.3	2.1
	N	10	10	10	10	10	10	10	10
GROUP 2									
4000 PPM	M	420.8	378.7	340.6	313.6	290.1	274.5	259.0	246.3
	SD	8.0	11.7	7.0	20.4	11.9	5.0	9.7	9.1
	N	10	10	9	10	10	10	10	10
GROUP 3									
16000 PPM	M	1664.0	1499.2	1358.4	1232.2	1186.9	1115.2	1065.4	1020.6
	SD	43.2	50.2	35.9	40.8	36.1	41.2	49.1	36.6
	N	10	10	10	10	10	10	10	10

BASF TOXICOLOGY
PROJECT NUMBER 30C0200/8625

3-MONTH FEEDING STUDY OF TCT IN RATS

GROUP MEANS

SUBSTANCE INTAKE

PRINT DATE 23-JUL-87

M A L E S		day 63	day 70	day 77	day 84	day 91
		SUB.INT. MG/KG BW	SUB.INT. MG/KG BW	SUB.INT. MG/KG BW	SUB.INT. MG/KG BW	SUB.INT. MG/KG BW
GROUP 1						
1000 PPM	M	59.0	57.1	57.5	54.2	53.1
	SD	3.1	2.6	4.9	1.7	1.8
	N	10	10	10	10	10
GROUP 2						
4000 PPM	M	236.2	230.0	225.7	220.4	215.0
	SD	12.0	14.9	15.2	8.5	4.1
	N	10	10	10	10	10
GROUP 3						
16000 PPM	M	985.6	946.9	929.1	888.7	882.4
	SD	19.7	24.2	31.6	29.9	45.3
	N	10	10	10	10	10

BASF TOXICOLOGY
PROJECT NUMBER 30C0200/8625

3-MONTH FEEDING STUDY OF TCT IN RATS

GROUP MEANS

SUBSTANCE INTAKE

PRINT DATE 23-JUL-87

F E M A L E S		day 7	day 14	day 21	day 28	day 35	day 42	day 49	day 56
		SUB.INT. MG/KG BW	SUB.INT. MG/KG BW	SUB.INT. MG/KG BW	SUB.INT. MG/KG BW	SUB.INT. MG/KG BW	SUB.INT. MG/KG BW	SUB.INT. MG/KG BW	SUB.INT. MG/KG BW
GROUP 1									
1000 PPM	M	105.4	94.6	89.7	82.3	81.5	77.7	76.7	74.0
	SD	4.2	3.6	4.3	4.8	6.4	4.0	5.4	4.1
	N	10	10	10	10	10	10	10	10
GROUP 2									
4000 PPM	M	436.6	390.3	367.9	337.1	335.4	321.6	321.6	300.6
	SD	17.9	19.4	17.8	16.1	13.9	15.3	17.5	11.0
	N	10	10	10	10	10	10	10	10
GROUP 3									
16000 PPM	M	1681.6	1523.4	1462.2	1377.0	1315.4	1207.0	1239.7	1206.4
	SD	38.8	69.1	53.3	47.8	79.7	46.1	54.0	50.2
	N	10	10	10	10	10	10	10	10

TABLE 020

BASF TOXICOLOGY
PROJECT NUMBER 30C0200/8625

3-MONTH FEEDING STUDY OF TCT IN RATS

GROUP MEANS

SUBSTANCE INTAKE

PRINT DATE 23-JUL-87

F E M A L E S		day 63	day 70	day 77	day 84	day 91
		SUB.INT. MG/KG BW	SUB.INT. MG/KG BW	SUB.INT. MG/KG BW	SUB.INT. MG/KG BW	SUB.INT. MG/KG BW
GROUP 1						
1000 PPM	M	73.0	71.0	70.7	70.6	67.9
	SD	6.0	3.9	4.4	4.4	4.7
	N	10	10	10	10	10
GROUP 2						
4000 PPM	M	294.1	289.0	286.6	273.7	270.2
	SD	18.3	12.8	20.8	12.8	11.8
	N	10	10	10	10	10
GROUP 3						
16000 PPM	M	1148.9	1090.9	1108.0	1128.8	1092.1
	SD	63.4	34.9	51.7	55.3	73.1
	N	10	10	10	10	10

TABLE 021

BASF TOXICOLOGY
PROJECT NUMBER 30C0200/8625

3-MONTH FEEDING STUDY OF TCT IN RATS

GROUP MEANS

HEMATOLOGY

PRINT DATE 12-AUG-87

Nominal days in study 93

M A L E S		WBC GIGA/L	RBC TERA/L	HGB MMOL/L	HCT L/L	MCV FL	MCH FMOL	MCHC MMOL/L	PLT GIGA/L
GROUP 0									
0 PPM	M	6.65	8.27	9.12	0.395	47.75	1.10	23.08	975
	SD	1.05	0.36	0.35	0.015	1.18	0.05	0.87	93
	N	10	10	10	10	10	10	10	9
GROUP 1									
1000 PPM	M	6.87	8.33	9.11	0.401	48.11	1.09	22.71	917
	SD	1.37	0.50	0.44	0.020	1.33	0.06	0.92	115
	N	10	10	10	10	10	10	10	10
GROUP 2									
4000 PPM	M	7.05	8.68	9.42	0.419	48.20	1.09	22.50	946
	SD	0.97	0.52	0.52	0.026	1.47	0.04	0.44	99
	N	10	10	10	10	10	10	10	9
GROUP 3									
16000 PPM	M	7.27	8.66	9.15	0.408	46.94	1.06	22.46	976
	SD	1.63	0.38	0.49	0.023	1.14	0.03	0.50	134
	N	10	10	10	10	10	10	10	10

Statistics: Anova + Dunnetts tests * P<0.05 ** P<0.01 two sided (Statistical unit = animal)

BASF TOXICOLOGY
PROJECT NUMBER 30C0200/8625 3-MONTH FEEDING STUDY OF TCT IN RATS

GROUP MEANS HEMATOLOGY PRINT DATE 30-SEP-87

Nominal days in study 93

F E M A L E S		WBC GIGA/L	RBC TERA/L	HGB MMOL/L	HCT L/L	MCV FL	MCH FMOL	MCHC MMOL/L	PLT GIGA/L
GROUP 0									
0 PPM	M	4.24	7.94	9.11	0.391	49.14	1.15	23.33	941
	SD	0.96	0.31	0.31	0.017	0.57	0.03	0.78	76
	N	10	10	10	10	10	10	10	8
GROUP 1									
1000 PPM	M	4.19	8.11	9.11	0.400	49.30	1.12	22.78	918
	SD	1.10	0.35	0.26	0.015	1.18	0.03	0.56	130
	N	10	10	10	10	10	10	10	9
GROUP 2									
4000 PPM	M	4.44	8.12	9.18	0.401	49.23	1.13	22.95	958
	SD	0.98	0.43	0.40	0.026	1.27	0.04	0.88	165
	N	10	10	10	10	10	10	10	9
GROUP 3									
16000 PPM	M	4.78	7.91	9.11	0.389	49.10	1.15	23.46	931
	SD	1.47	0.38	0.24	0.018	0.80	0.05	1.12	92
	N	10	10	10	10	10	10	10	9

Statistics: Anova + Dunnetts tests * P<0.05 ** P<0.01 two sided (Statistical unit = animal)

TABLE 023

BASF TOXICOLOGY
PROJECT NUMBER 30C0200/8625

3-MONTH FEEDING STUDY OF TCT IN RATS

GROUP MEANS

DIFFERENTIAL BLOOD COUNT

Nominal days in study 93

M A L E S		EOS %	BASO %	META %	BAND %	POLY %	LYMP %	MONO %
GROUP 0								
0 PPM	M	1.40	0.20	0.20	0.00	13.00	80.40	4.80
	SD	0.97	0.42	0.42	0.00	4.11	3.81	1.14
	N	10	10	10	10	10	10	10
GROUP 1								
1000 PPM	M	1.80	0.00	0.00	0.00	7.50	84.50	6.20
	SD	1.03	0.00	0.00	0.00	1.43	3.41	2.44
	N	10	10	10	10	10	10	10
GROUP 2								
4000 PPM	M	2.20	0.00	0.10	0.00	9.40	81.60	6.70
	SD	1.14	0.00	0.32	0.00	4.12	4.45	3.20
	N	10	10	10	10	10	10	10
GROUP 3								
16000 PPM	M	2.60	0.10	0.10	0.00	10.60	81.80	4.80
	SD	0.97	0.32	0.32	0.00	3.50	4.92	1.81
	N	10	10	10	10	10	10	10

BASF TOXICOLOGY
PROJECT NUMBER 30C0200/8625

3-MONTH FEEDING STUDY OF TCT IN RATS

GROUP MEANS

DIFFERENTIAL BLOOD COUNT

Nominal days in study 93

M A L E S		WBC GIGA/L	EOS GIGA/L	BASO GIGA/L	META GIGA/L	BAND GIGA/L	POLY GIGA/L	LYMP GIGA/L	MONO GIGA/L
GROUP 0									
0 PPM	M	6.65	0.09	0.01	0.01	0.00	0.86	5.35	0.32
	SD	1.05	0.06	0.03	0.03	0.00	0.31	0.91	0.09
	N	10	10	10	10	10	10	10	10
GROUP 1									
1000 PPM	M	6.87	0.12	0.00	0.00	0.00	0.51	5.80	0.43
	SD	1.37	0.08	0.00	0.00	0.00	0.14	1.18	0.20
	N	10	10	10	10	10	10	10	10
GROUP 2									
4000 PPM	M	7.05	0.15	0.00	0.01	0.00	0.68	5.74	0.46
	SD	0.97	0.06	0.00	0.03	0.00	0.36	0.74	0.18
	N	10	10	10	10	10	10	10	10
GROUP 3									
16000 PPM	M	7.27	0.19	0.01	0.01	0.00	0.75	5.96	0.36
	SD	1.63	0.07	0.02	0.03	0.00	0.23	1.42	0.16
	N	10	10	10	10	10	10	10	10

TABLE 025

BASF TOXICOLOGY
PROJECT NUMBER 30C0200/8625

3-MONTH FEEDING STUDY OF TCT IN RATS

GROUP MEANS

DIFFERENTIAL BLOOD COUNT

Nominal days in study 93

F E M A L E S		EOS %	BASO %	META %	BAND %	POLY %	LYMP %	MONO %
GROUP 0								
0 PPM	M	3.40	0.20	0.00	0.20	13.00	79.70	3.50
	SD	1.90	0.42	0.00	0.42	5.54	4.79	1.43
	N	10	10	10	10	10	10	10
GROUP 1								
1000 PPM	M	2.30	0.00	0.00	0.00	10.40	82.30	5.00
	SD	2.06	0.00	0.00	0.00	4.50	5.40	2.71
	N	10	10	10	10	10	10	10
GROUP 2								
4000 PPM	M	1.80	0.00	0.00	0.00	11.50	83.60	3.10
	SD	1.03	0.00	0.00	0.00	7.65	6.65	2.18
	N	10	10	10	10	10	10	10
GROUP 3								
16000 PPM	M	2.00	0.00	0.00	0.00	12.60	81.50	3.90
	SD	1.63	0.00	0.00	0.00	6.67	6.11	1.66
	N	10	10	10	10	10	10	10

BASF TOXICOLOGY
PROJECT NUMBER 30C0200/8625

3-MONTH FEEDING STUDY OF TCT IN RATS

GROUP MEANS

DIFFERENTIAL BLOOD COUNT

Nominal days in study 93

F E M A L E S		WBC GIGA/L	EOS GIGA/L	BASO GIGA/L	META GIGA/L	BAND GIGA/L	POLY GIGA/L	LYMP GIGA/L	MONO GIGA/L
GROUP 0									
0 PPM	M	4.24	0.14	0.01	0.00	0.01	0.55	3.38	0.15
	SD	0.96	0.08	0.02	0.00	0.02	0.25	0.81	0.06
	N	10	10	10	10	10	10	10	10
GROUP 1									
1000 PPM	M	4.19	0.09	0.00	0.00	0.00	0.43	3.45	0.23
	SD	1.10	0.08	0.00	0.00	0.00	0.17	0.96	0.15
	N	10	10	10	10	10	10	10	10
GROUP 2									
4000 PPM	M	4.44	0.08	0.00	0.00	0.00	0.51	3.72	0.14
	SD	0.98	0.05	0.00	0.00	0.00	0.37	0.92	0.10
	N	10	10	10	10	10	10	10	10
GROUP 3									
16000 PPM	M	4.78	0.08	0.00	0.00	0.00	0.58	3.92	0.20
	SD	1.47	0.06	0.00	0.00	0.00	0.32	1.35	0.13
	N	10	10	10	10	10	10	10	10

BASF TOXICOLOGY
PROJECT NUMBER 30C0200/8625

3-MONTH FEEDING STUDY OF TCT IN RATS

GROUP MEANS

CLOTTING ANALYSIS

PRINT DATE 12-AUG-87

Nominal days in study 93

M A L E S		HQT SECONDS
GROUP 0		
0 PPM	M	41.4
	SD	1.7
	N	9
GROUP 1		
1000 PPM	M	39.1
	SD	5.5
	N	10
GROUP 2		
4000 PPM	M	39.8
	SD	3.3
	N	10
GROUP 3		
16000 PPM	M	38.8
	SD	5.7
	N	10

Statistics: Anova + Dunnetts tests * P<0.05 ** P<0.01 two sided (Statistical unit = animal)

BASF TOXICOLOGY
PROJECT NUMBER 30C0200/8625

3-MONTH FEEDING STUDY OF TCT IN RATS

PRINT DATE 12-AUG-87

GROUP MEANS

CLOTTING ANALYSIS

Nominal days in study 93

F E M A L E S		HQT SECONDS
GROUP 0		
0 PPM	M	37.3
	SD	2.4
	N	9
GROUP 1		
1000 PPM	M	36.3
	SD	3.5
	N	10
GROUP 2		
4000 PPM	M	35.8
	SD	3.9
	N	10
GROUP 3		
16000 PPM	M	38.5
	SD	1.6
	N	9

Statistics: Anova + Dunnetts tests * P<0.05 ** P<0.01 two sided (Statistical unit = animal)

BASF TOXICOLOGY
PROJECT NUMBER 30C0200/8625

3-MONTH FEEDING STUDY OF TCT IN RATS

GROUP MEANS

ENZYMES

PRINT DATE 12-AUG-87

Nominal days in study 93

M A L E S		ALT MYKAT/L	AST MYKAT/L	ALP MYKAT/L
GROUP 0				
0 PPM	M	0.89	2.32	4.95
	SD	0.20	0.65	0.85
	N	10	10	10
GROUP 1				
1000 PPM	M	0.76	2.05	5.20
	SD	0.14	0.57	0.54
	N	10	10	10
GROUP 2				
4000 PPM	M	0.82	1.93	5.49
	SD	0.10	0.42	0.88
	N	10	10	10
GROUP 3				
16000 PPM	M	0.97	2.22	5.30
	SD	0.11	0.29	0.52
	N	10	10	10

Statistics: Anova + Dunnetts tests * P<0.05 ** P<0.01 two sided (Statistical unit = animal)

BASF TOXICOLOGY
PROJECT NUMBER 30C0200/8625

3-MONTH FEEDING STUDY OF TCT IN RATS

GROUP MEANS

ENZYMES

PRINT DATE 12-AUG-87

Nominal days in study 93

F E M A L E S		ALT MYKAT/L	AST MYKAT/L	ALP MYKAT/L
GROUP 0				
0 PPM	M	0.74	2.66	4.20
	SD	0.15	0.61	0.99
	N	10	10	10
GROUP 1				
1000 PPM	M	0.68	1.89	4.14
	SD	0.15	0.59	0.72
	N	10	10	10
GROUP 2				
4000 PPM	M	0.76	2.53	4.33
	SD	0.17	1.01	0.61
	N	10	10	10
GROUP 3				
16000 PPM	M	0.84	3.11	3.95
	SD	0.46	2.27	0.76
	N	10	10	10

Statistics: Anova + Dunnetts tests * P<0.05 ** P<0.01 two sided (Statistical unit = animal)

BASF TOXICOLOGY
PROJECT NUMBER 30C0200/8625

3-MONTH FEEDING STUDY OF TCT IN RATS

GROUP MEANS

BLOOD CHEMISTRY

PRINT DATE 12-AUG-87

Nominal days in study 93

M A L E S		NA MMOL/L	K MMOL/L	CL MMOL/L	INP MMOL/L	CA MMOL/L	UREA MMOL/L	CREA MYMOL/L	GLUC MMOL/L
GROUP 0									
0 PPM	M	142.60	6.37	108.65	2.26	2.78	6.70	52.74	7.07
	SD	2.36	0.58	4.30	0.17	0.12	0.44	4.82	0.75
	N	10	10	10	10	10	10	10	10
GROUP 1									
1000 PPM	M	142.55	5.98	109.29	2.25	2.76	7.33*	52.74	7.06
	SD	2.33	0.72	4.58	0.23	0.09	0.74	4.01	0.62
	N	10	10	10	10	10	10	10	10
GROUP 2									
4000 PPM	M	142.50	6.26	108.42	2.44	2.82	6.82	52.23	6.62
	SD	2.65	0.49	3.21	0.18	0.14	0.54	1.95	0.55
	N	10	10	10	10	10	10	10	10
GROUP 3									
16000 PPM	M	143.73	6.17	109.42	2.35	2.80	6.72	55.90	7.98
	SD	4.75	0.76	5.23	0.34	0.20	0.33	2.84	2.19
	N	10	10	10	10	10	10	10	10

Statistics: Anova + Dunnetts tests * P<0.05 ** P<0.01 two sided (Statistical unit = animal)

BASF TOXICOLOGY
PROJECT NUMBER 30C0200/8625

3-MONTH FEEDING STUDY OF TCT IN RATS

GROUP MEANS

BLOOD CHEMISTRY

PRINT DATE 12-AUG-87

Nominal days in study 93

M A L E S		TBIL MYMOL/L	TPROT G/L	ALB G/L	GLOB G/L	TRIG MMOL/L	CHOL MMOL/L
GROUP 0							
0 PPM	M	3.39	68.22	32.03	36.18	2.92	2.16
	SD	0.55	3.37	1.11	2.53	0.69	0.23
	N	10	10	10	10	10	10
GROUP 1							
1000 PPM	M	3.12	67.66	32.76	34.90	4.77*	2.16
	SD	0.83	2.56	1.05	2.24	1.97	0.22
	N	10	10	10	10	10	10
GROUP 2							
4000 PPM	M	2.83	68.62	33.05	35.58	4.62*	2.27
	SD	0.68	3.08	1.79	2.15	1.03	0.39
	N	10	10	10	10	10	10
GROUP 3							
16000 PPM	M	3.72	69.45	32.93	36.53	3.10	2.12
	SD	0.82	4.55	1.58	3.30	1.37	0.24
	N	10	10	10	10	10	10

Statistics: Anova + Dunnetts tests * P<0.05 ** P<0.01 two sided (Statistical unit = animal)

BASF TOXICOLOGY
PROJECT NUMBER 30C0200/8625

3-MONTH FEEDING STUDY OF TCT IN RATS

GROUP MEANS

BLOOD CHEMISTRY

PRINT DATE 12-AUG-87

Nominal days in study 93

F E M A L E S		NA MMOL/L	K MMOL/L	CL MMOL/L	INP MMOL/L	CA MMOL/L	UREA MMOL/L	CREA MYMOL/L	GLUC MMOL/L
GROUP 0									
0 PPM	M	143.21	5.75	113.00	1.93	2.64	6.88	57.40	7.01
	SD	3.17	0.42	5.24	0.25	0.12	0.82	5.44	0.95
	N	10	10	10	10	10	10	10	10
GROUP 1									
1000 PPM	M	141.43	5.81	111.60	2.00	2.65	6.95	53.23	7.11
	SD	3.41	0.71	2.97	0.19	0.14	1.27	3.34	0.77
	N	10	10	10	10	10	10	10	10
GROUP 2									
4000 PPM	M	141.59	5.66	113.67	2.17	2.77*	7.40	54.72	6.80
	SD	3.84	0.55	5.50	0.29	0.14	0.96	3.97	0.44
	N	10	10	10	10	10	10	10	10
GROUP 3									
16000 PPM	M	143.01	5.47	113.15	1.89	2.60	6.44	57.73	7.18
	SD	3.35	0.41	5.02	0.20	0.06	0.82	4.65	0.90
	N	10	10	10	10	10	10	10	10

Statistics: Anova + Dunnetts tests * P<0.05 ** P<0.01 two sided (Statistical unit = animal)